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BIOCOMPATIBLE FLUORESCENT MICROSPHERES: SAFE PARTICLES FOR MATERIAL PENETRATION STUDIES (TAS Review Brief)

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BIOCOMPATIBLE FLUORESCENT MICROSPHERES: SAFE PARTICLES FOR MATERIAL PENETRATION STUDIES (TAS Review Brief)

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Hypothesis and Goals:

The use of biocompatible polymer microspheres has been proposed for use in drug delivery, dispersal model verification and as a surrogate for threat agents in instrument validation [1,2]. Modifying the production methods used in drug delivery for aerosol production should allow for low cost bio-weapon simulants. The ability to have a polymer sphere with a broad range of property tuning will allow for safe low cost use for homeland security and defense applications. Three main challenges are present in the production of such spheres. The first challenge is the reproduction of the fluorescent and other chemical properties of interest. Secondly, the particles must have the size and charge attributes needed for the specific application and testing. Finally, in order to reproduce testing and evaluation criteria a rapid, reliable, scalable and low cost production method must be available.

Methods:

Particle Production:

Several different microsphere preparation methods were evaluated, including the use of a vibrating orifice aerosol generator (VOAG), a Sono-Tek atomizer, an emulsion technique, and a COTS inkjet printhead.

Fluorescence:

The spheres were tested with total luminescence spectroscopy (TLS) for ability to simulate a threat agent fluorescence spectrum. TLS is commonly used as excitation emission matrices where both the excitation and intensity of the emission are recorded. This measurement results in a unique matrix that can be used to fingerprint and identify the fluorescent compound. Multiple materials were tested to determine the suitability to simulate the fluorescent properties of threat agents. TLS libraries were also made for a viariety of threats including B. *anthracis stern*, *B anthracis ames* and *Y. Pestis.*

Size Determination:

Several commercially available techniques are available for aerosol size measurement in the 1-10μm size range. The microsphere size profile was measured with an Aerosol Particle Sizer (APS), SEM, and LLNL's Single Particle Aerosol Mass Spectrometer.

Charge:

Particle charge was measured with the charge detector recently developed by the Single Particle Aerosol Mass Spectrometry Group at LLNL. A single particle enters a conductive tube and induces a charge on the tube. The mirror image charge is amplified and recorded.

Achievements and Future Work:

The production of bio-safe micro-spheres with a VOAG[3], Sono-Tek[4] and emulsion[5] techniques were demonstrated to reproduce many of the desired characteristics of a simulated threat agent. By using tryptophan and poly-tryptophan as the only fluorophore a close match to the TLS of *B. anthracis* was achieved. Fine-tuning of the fluorescent properties with additional chemicals should prove the ability to match most if not all threat agents.

The tested methods show the ability to produce particles in a size range that would be applicable for threat agent simulants. However, with poly-dispersed methods such as the emulsion technique, and Sono-Tek aerosol generator costly and time consuming size sorting would be required. The VOAG has the capability of producing a mono-dispersed particle type but has significant drawbacks in the ability to mass-produce particles at a low cost. Commercial ink jet print heads allow for a tight size distribution in the desired 1-3 micron size range at a very low cost and with production scalability.

In addition to the work shown in this report the research has given insight into some future research aspects. It has been proposed that by using food based simulant particles a safe inhalable simulant can be produced. Currently this is being explored using gluco-delta-lactone FDA approved food products. It is intended that the new research area will also incorporate DNA into the particles for use in the Pentagon Shield program.

REFERENCES:

1 Author(s): Freiberg, S; Zhu, X, 'Polymer microspheres for controlled drug release', INTERNATIONAL JOURNAL OF PHARMACEUTICS, 282 (1-2): 1-18 SEP 10 2004

2 Fletcher, RA (Fletcher, Robert A.); Brazin, JA (Brazin, Jacquelyn A.); Staymates, ME (Staymates, Matthew E.); Benner, BA (Benner, Bruce A., Jr.); Gillen, JG (Gillen, J. Greg), "Fabrication of polymer microsphere particle standards containing trace explosives using an oil/water emulsion solvent extraction piezoelectric printing process", Source: TALANTA, 76 (4): 949-955 AUG 15 2008

3 http://www.tsi.com/Product.aspx?Pid=58 accessed 9-14-08

4 http://www.sono-tek.com/ accessed 9-14-08

5 Jain, R; Shah, NH; Malick, AW; Rhodes, CT, "Controlled drug delivery by biodegradable poly(ester) devices: Different preparative approaches",